Translation

PATENT COOPERATION TREATY

PCT/JP2003/013259

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 1513	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/JP2003/013259	International filing date (*day/month/year*) 16 October 2003 (16.10.2003)	Priority date (*day/month/year*) 16 October 2002 (16.10.2002)
International Patent Classification (IPC) or national classification and IPC C12Q 1/60, 1/26, 1/32, 1/44, G01N 33/92, C07J 1/00		
Applicant KYOWA MEDEX CO., LTD.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the report
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14 May 2004 (14.05.2004)	10 November 2004 (10.11.2004)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

national application No.
PCT/JP2003/013259

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ The international application as originally filed/furnished

☐ the description:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

pages _____, as originally filed/furnished

pages* _____, as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the drawings:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

national application No.
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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☒ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   See supplemental sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☒ all parts.

   ☐ the parts relating to claims Nos. _____

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: IV. 3.

The inventions set forth in claims 1-10, 12-23 and 25-39 are a group of inventions which address the problem of offering an improved method for simple and accurate measurement of high-density lipoprotein-bound cholesterol, and measurement reagents and kits for the purpose thereof.

By contrast, the inventions set forth in claims 11, 24 and 40-42 are a group of inventions which address the problem of offering compounds described in claim 41.

The two groups of inventions address different problems; therefore, these groups of inventions do not constitute a group of inventions so linked as to form a single general inventive concept.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP 03/13259

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	2,8-11,15,21-24,26-31,37-42	YES
	Claims	1,3-7,12-14,16-20,25,32-36	NO
Inventive step (IS)	Claims	11, 24, 40-42	YES
	Claims	1-10, 12-23, 25-39	NO
Industrial applicability (IA)	Claims	1-42	YES
	Claims		NO

2. Citations and explanations

Document 1: JP 08-116996 A (Toyobo Co., Ltd.), 14 May 1996

Document 2: WO 97/40376 A1 (Iatron Lab. Inc.), 30 October 1997

Document 3: JP 11-009300 A (Iatron Lab. Inc.), 19 January 1999

Document 4: WO 95/24502 A1 (Kyowa Medex Co., Ltd.), 14 September 1995

1. The inventions set forth in claims 1, 3-7, 12-14, 16-20, 25 and 32-36 are not novel and do not involve an inventive step in the light of inventions disclosed in documents 1-3, cited in the international search report.

Document 1 discloses a method for measuring high-density lipoprotein (HDL) cholesterol characterized in that the specimen to be tested is reacted with cholesterol ester hydrolase and (chemically modified) cholesterol oxidase in an aqueous medium containing a bile acid derivative having an anionic surfactant action (such as dehydrocholic acid), and the hydrogen peroxide produced is measured, and also discloses reagents (a kit) for measuring high-density lipoprotein (HDL) cholesterol which contain reagents used in said method of measurement, with

said reagents comprising a first reagent and a second reagent, wherein the cholesterol ester hydrolase and the bile acid derivative are contained in the first reagent, the cholesterol oxidase or cholesterol dehydrogenase is contained in the second reagent, and the reagent for measuring hydrogen peroxide is contained in the first reagent or the second reagent.

Therefore, the inventions set forth in claims 1, 3-7, 12-14, 16-20, 25 and 32-36 are substantially the same as the inventions disclosed in document 1.

2. Claims 2, 8-10, 15, 21-23, 26-31 and 37-39 do not involve an inventive step in the light in the light of inventions disclosed in documents 1-3, cited in the international search report.

Document 2 (see especially claims 1 and 6 and the section on background art in the detailed description of the invention) discloses reagents containing a bile acid or salt thereof, albumin, a non-ionic surfactant, cholesterol ester hydrolase, cholesterol oxidase and a reagent for measuring hydrogen peroxide, as reagents specific for the measurement of high-density lipoprotein (HDL) cholesterol (kit), and indicates that an anionic bile acid derivative such as taurocholic acid or glycocholic acid can be used as the bile acid; it also discloses a method for specific measurement of high-density lipoprotein (HDL) cholesterol using said reagents wherein the cholesterol ester hydrolase, cholesterol oxidase and bile acid (derivative) are brought into contact with the specimen in the presence of albumin, and indicates that by this method, namely bringing the test specimen into contact with the enzymes in the presence of albumin, it is possible to inhibit reaction between the

enzymes and LDL-cholesterol and VLDL-cholesterol in the specimen while reaction between the enzymes and HDL-cholesterol proceeds unimpeded.

It was well known in the art at the time of filing the present application that in general in order to measure high-density lipoprotein (HDL) cholesterol reliably, conditions in which there is as nearly as possible no reaction of the enzymes with LDL cholesterol and VLDL cholesterol present in the specimen (inhibition) are desirable.

Given this a person skilled in the art could easily conceive of applying the invention disclosed in document 2, and bring the enzymes and the specimen into contact in the presence of albumin, in the method for measuring high-density lipoprotein (HDL) cholesterol and measurement reagents (kit) for this purpose disclosed in document 1, applying the aforementioned commonly known fact so as to ensure the aforementioned conditions, namely to inhibit reaction between the enzymes and LDL-cholesterol and VLDL-cholesterol in the specimen, while allowing the reaction between the enzymes and HDL-cholesterol to proceed unimpeded, with the object of accurate measurement of HDL cholesterol.

In addition, document 3 discloses the possibility of using a compound represented by R1-CH2-CH(R2)-CH2-SO3- (R1 is a 3-(3-cholamidopropyl)dimethylammonio group and R2 is a hydrogen atom or a hydroxyl group) which acts as an amphoteric surfactant, as a bile acid derivative used in a specific method for measuring cholesterol.

Given this, using a compound represented by R1-CH2-CH(R2)-CH2-SO3- (R1 is a 3-(3-cholamidopropyl)dimethyl-ammonio group and R2 is a hydrogen atom or a hydroxyl group) which acts as an amphoteric surfactant, disclosed

in document 3 as a bile acid derivative used in a specific method for measuring cholesterol, in the method for measuring HDL-cholesterol and measurement reagents (kit) for this purpose disclosed in document 1, also does not involve any special difficulty.

3. The inventions set forth in claims 11, 24 and 40-42 are not disclosed in any of documents 1-4 above, cited in the international search report, and are novel and involve an inventive step.